Glucosamine Chondroitin Plus is a well-balanced formulation with both nutritive and pharmacologically active properties.

It contains Glucosamine sulfate to promote the formation and repair of cartilage. Chondroitin sulfate helps to promote water retention and elasticity of cartilage and inhibits enzymes that degrade cartilage. This formula also includes the additional nutritive and anti-inflammatory properties of *Perna canaliculus* (green-lipped mussel) and the analgesic and tonifying action of *Harpagophytum procumbens* (devil’s claw).

**Product highlight**

A highly effective product with active ingredients that not only reduce joint inflammation but provide regenerative and protective properties for healthy joint, cartilage and connective tissue formation.

**Active ingredients**

- Glucosamine sulphate 750mg
- Chondroitin sulphate 250mg
- *Perna canaliculus* (green lipped mussel) powder 75mg
- *Harpagophytum procumbens* (Devil’s Claw) 200mg

**Recommended Adult Dose**

Adults – Take one tablet three times daily with food or as directed by your healthcare practitioner.

**Pregnancy and Breast Feeding**

No adverse affects known.

**Warning**

Glucosamine sulfate is derived from shellfish. May cause hypersensitivity reactions in susceptible individuals.

**Indications**

- Temporary relief of the pain of arthritis
- May help reduce joint inflammation associated with arthritis
- May reduce joint swelling associated with arthritis

**Conditions**

<table>
<thead>
<tr>
<th>Arthrosis</th>
<th>Lower lumbar pain</th>
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<td>Osteoarthritis</td>
<td>Sport/exercise induced joint injury</td>
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**Overview**

The incidence of arthritis worldwide and the ensuing burden of disease has been an issue of escalating concern for governments and healthcare providers. The medical treatment of disease has to date relied on anti-inflammatory agents with a questionable safety protocol. The recent concern over, and subsequent withdrawal of selective COX – 2 inhibitors from the marketplace has driven home this issue. It has also brought to the attention of medical authorities the need for safer disease modifying agents. These agents would need to provide symptomatic relief, without the harmful side effects profile associated with many of the anti-inflammatory drugs currently available (both prescription and over-the-counter). They would also need to impede degeneration and even improve tissue function. Which is where glucosamine and chondroitin come into the picture.

Both these agents have developed a strong reputation for their remarkable efficacy in the treatment of inflammatory and degenerative conditions such as rheumatoid arthritis and osteoarthritis. The results of numerous in vitro and in vivo studies have supported and substantiated the faith in these agents, whose supporting data were largely empirical/anecdotal to date.

These results have been so impressive in fact, that glucosamine sulfate either alone or in combination with chondroitin sulfate, is now being considered as the first line of treatment in arthritis.

Other important agents include traditional botanicals such as *Harpagophytum procumbens* (devil’s claw). Devil’s claw has demonstrated anti-inflammatory and analgesic properties and is also a
powerful bitter tonic. Impressive results have also been obtained with extracts of green lipped mussel extract. In combination with GS and CS, they provide nutritive and pharmacoactive properties which have an additive (and possibly synergistic) effect which serves to widen the application of these formulations to a range of conditions.

**Glucosamine Sulfate**

Glucosamine sulfate is a naturally occurring amino sugar, a simple molecule composed of glucose bonded to an amine (a combination of glutamine and glucose combined with a sulfate group).

Glucosamine sulfate is found in many tissues and body fluids.

There are no dietary sources of glucosamine, and it is usually derived from chitin, which is obtained from raw materials derived from animal sources (marine).

The body’s failing ability to manufacture glucosamine, may be the key-contributing factor in the pathogenesis of arthritis. The role of Glucosamine sulfate in slowing or reversing joint degeneration appears to be directly due to its ability to act as an primary amino sugar substrate for, and also stimulating the biosynthesis of, the glycosaminoglycans, glycolipids, glycoproteins, and the hyaluronic acid backbone needed for the formation of the proteoglycans found in the structural matrix of joints. (Alt Med Review 1999)

Glucosamine is very soluble in water. It is well absorbed when administered via the oral route (90%). It is believed that glucosamine delivery to cells is carrier mediated (actively transported). Glucosamine is rapidly incorporated into articular cartilage following oral administration (Kelly 1998).

**Chondroitin**

Chondroitin sulfate (CS) is a predominant component of the extracellular matrix of many connective tissues. These include cartilage, bone, skin, ligaments, and tendons. CS is a sulfated glycosaminoglycan. It is composed of a long unbranched polysaccharide chain with a repeating disaccharide structure of N-acetylgalactosamine and glucuronic acid. (Lippiello L et al 2000)

Most of the N-acetylgalactosamine residues are sulfated. This makes CS a strongly charged polyanion with a high water-draining power.

In the articular cartilage, the high content of CS in the aggregan plays a major role in creating a large osmotic swelling pressure that expands the matrix and places the collagen network under tension. (Jean-Yves Reginster et al 2003)

**Absorption**

Unlike Glucosamine sulfate, Chondroitin sulfate is not as well absorbed, although the subject remains controversial. It is widely accepted that molecules with a high molecular mass and charge density cannot pass through the gastric and intestinal mucosa without first being modified for absorption, although it has been shown that in some instances, up to 8.5% of intact CS can be absorbed. It is also quite possible that, “the majority of the physiological benefits appear to be a direct result of increased availability of monosaccharide building blocks (glucuronic acid and N-acetylgalactosamine) created by the hydrolysis of CS into smaller molecules during digestion and absorption.” (Kelly 1998)

Chondroitin has a protective effect on cartilage and attracts fluids that give the tissue its shock absorbing quality. Chondrocytes in degenerating discs have insufficient capacity to make functional proteoglycans with the correct sulfation for sufficient water retention.

It is likely that the diffusion of nutrients is facilitated by moderate intermittent hydrostatic pressure, e.g. during physical exercise.

When there is excessive or prolonged load on the intervertebral joints this can cause injuries that affect disc integrity.

Disc degeneration begins around the vertebral endplate, often after impairment of the vascular bed system, which interrupts nutrition via the vertebral route. This combined with ageing and/or genetic factors, promotes the breakdown of proteoglycans and other changes in the disc.

The eventual result of this imbalance in molecular turnover is matrix resorption and dehydration of the nucleus and of the annulus fibrosus, resulting in reduction of disc height and further progression of
the degeneration process, leading to clinical symptoms such as lower back pain. (van Blitterswijk et al. 2003)

### Glucosamine
- Stimulates the biosynthesis of the glycosaminoglycans, glycolipids, glycoproteins, and hyaluronic acid
- Increases production of new cartilage molecules (called aggrecans)
- Decreases production of enzymes that degrade cartilage (matrix metalloproteinases 1 and 3)
- Increases cartilage cell (chondrocyte) adhesion when cartilage becomes fibrillated
- Suppresses production of nitric oxide (which can cause early cartilage cell death)
- Glucosamine can inhibit the COX-2 enzyme without affecting COX-1.

### Chondroitin Sulfate
- Increases the synthesis of hyaluronan by chondrocyte-derived fibroblast-like cells
- Increases the synthesis rates and the accumulation of aggrecan
- Increases matrix component production by human chondrocytes and inhibits the negative effects of interleukin-1b
- Increases synovial fluid viscosity
- Restoration of the sulfated proteoglycan matrix leads to more water retention to improve hydraulic cushioning
- Inhibits extracellular proteases involved in cartilage degradation
- Anti-inflammatory effect which protects cartilage against damage from free radicals
- Shows a mild anti-inflammatory effect
- Inhibits collagenase and elastase production by chondrocytes.

### Possible Synergistic or Additive Affect
At this stage it has been demonstrated in animal models, that combined Glucosamine and Chondroitin Sulfate is more effective than the compounds administered singly. Clinical studies in animals and man have further indicated that the combination therapy is effective, and allows a significant drop in NSAID use by osteoarthritis patients.

The current understanding is that oral glucosamine and Chondroitin Sulfate can pass the gastrointestinal tract and reach articular cartilage. It is also possible for these compounds to reach intervertebral discs. They most likely have chondroprotective as well as a regenerative effect on joint tissue. In a study conducted in Queensland using a combination of green lipped mussel and celery seed, it was observed that combinations of nutriceuticals may, “amplify the potency and reduce the gastrotoxic and lymphopenic side effects” of both steroidal and non steroidal anti-inflammatories. (Whitehouse MW, Butters DJ. 2003)

### Glucosamine Dose
In a review of the evidence currently available of for Glucosamine sulfate in OA, a dose of 1500 mg/day has been demonstrated to achieve beneficial regenerative effects and to help ameliorate symptoms. (Jack J, 2002)

### Why Sulfates?
Sulfur is an essential nutrient for the stabilization of the connective tissue matrix. Sulfate depletion can lead to a decrease of glycosaminoglycan synthesis in patellar cartilage. (van de Kran et al 1988) Articular cartilage is sensitive to small changes in physiological sulphur concentrations. The recent addition of organic sulfur compounds such as MSM (Methyl sulphonyl methane) to formulations would seem to support this understanding. Most sulfur compounds are synthesized from the parent compound methionine. (Parcell 2002)

Sulfur is depleted in articular cartilage by anti-inflammatory agents used to treat Rheumatoid arthritis and Osteoarthritis. (van de Kran et al 1988) Sulfur can also decrease the toxicity of acetaminophen, although it is also known to reduce the drug’s analgesic effect. (Levy et al 1986)

The use of organic sulfur (both topical and ingested) is well established in naturopathic medicine for the treatment of skin conditions. And chondroitin sulfate could well be a useful treatment for skin conditions in the future. A recent ‘serendipidous finding’ has highlighted the potential of chondroitin sulfate in this area. Results of a study conducted in Spain in 2005 (during treatment for osteoarthritis) met with an astounding result. According to the researchers, “all patients but one presented a dramatic improvement of the condition.
of the skin, with a reduction of swelling, redness, flaking, and itching (clearance of psoriasis in one patient), increase in the hydration and softening of the skin, and amelioration of scaling.” (Verges J et al 2005).

Devil’s Claw
Although the compounds responsible and the action of Devil’s claw are yet to be thoroughly elucidated, some key constituents and their therapeutic properties have been identified. According to Weiss (1988), “the main constituents are three glycosides belonging to the iridoid group: herpagoside, harpagide and procombide, also a phytosterol mixture consisting mainly of beta-sitosterol and stigmasterol, unsaturated fatty acids (cinnamic acid, chlorogenic acid) — a comprehensive mixture of active principles. Devil’s claw has a characteristically bitter taste. In the traditional setting (African indigenous medicine) it was used as a purgative and bitter tonic.

It was also used as an analgesic. In Traditional Western herbal medicine uses include: Rheumatism, arthritis, gout, myalgia and lumbago. It was also used as a general tonic, as a digestive stimulant, and for digestive disorders. (Bone 2003)

In vitro studies (as injection) have identified an analgesic effect comparable to aspirin, although this has not been established with oral doses. According to some researchers, the active harpagosides (iridoid glycosides) are not responsible for the analgesic benefits of devils claw. “The main iridoid glycoside of H. procumbens appears to be implicated in the peripheral analgesic properties of this species, but other compounds have to be involved, since the dose of 10 mg/kg exerted a significant protective effect.” (Chrubasik 2002)

The results of these studies demonstrate that Harpagophytum extracts with >50 mg harpagoside per day are helpful in alleviating pain. According to the ESCOP monograph up to 9 g of crude drug with not less than 1% harpagoside is recommended for painful arthropathy and tendonitis — a dose that contains up to 90 mg of harpagoside. In placebo controlled, double blind studies, which employed 335 and 400mg (iridoid glycosides 1.5 and 3%) showed considerable improvement in pain intensity and mobility. (Long, Soeken and Ernst 2001).

According to Chrubasik (2002), “it is likely that the ethanol extraction selects a range of less polar but more effective substances than does aqueous extraction, so it is possible that these putative substances are present in a greater proportion to harpagoside in ethanol extracts than in aqueous extracts.”

Green Lipped Mussel
Green lipped mussel (Perna canaliculus) is a powdered extract of the flesh of New Zealand or Australian green lipped mussels. Green lipped mussel is well suited to formulations that contain Glucosamine and chondroitin, as it contains similar compounds, particularly the glycosaminoglycans (GAGS). Carbohydrate chains made primarily of alternating of either NAG (N-acetylgalactosamine) plus glucuronic acid or its epimer iduronic acid.

Experimental studies have shown that the New Zealand green lipped mussel (Perna canaliculus) is effective at inhibiting 5'-lipoxygenase and cyclooxygenase pathways, which are responsible for the production of eicosanoids, including leukotrienes and prostaglandins. The extract (Lyprinol) was shown to be rich in eicosapentaenoic acid and docosahexanoic acid, ω-3 fatty acids that inhibit the metabolism of arachidonic acid. This extract was shown to be effective in reducing pain, swelling and stiffness and in improving the functional index in patients with rheumatoid arthritis and osteoarthritis. Veterinary studies have yielded encouraging results using green-lipped mussel extract to treat arthritis in dogs. (Bui, LM Bierer TL 2003)

Companion Formulae
SAMe, Osteoapatite with Boron.

Complementary Considerations
Low Reactive Diet
A low reactive diet is an important way of reducing pain and inflammation thus avoiding the need for analgesics and anti inflammatory drug interventions. This will also increase the effectiveness of agents such as glucosamine and chondroitin.

- Consume low glycemic index foods to avoid insulin resistance
- Reduce/rotate gluten containing grains
- Eliminate white flour products
- Reduction or elimination of canned, pre-packaged and frozen foods (canned fish may contain fatty acids such as EPA and DHA but they in lower concentrations compared to the fresh variety. Canned foods are devoid of enzyme activity, which can place a burden on the pancreas).
- At least 3 fresh fish meals per week
- Fresh vegetable juices daily (vary combinations, could include carrot, apple, ginger, celery, parsley etc)
- Avoid pork (Arachadonic acid)
- Reduce beef intake
- Avoid cured ‘deli’ meats (nitrite are converted to nitrosamines)
- Keep alcohol to minimum (max two standard glasses daily)
- Avoid nuts (unless freshly shelled) as they have the potential for toxicity, rancidity, and maldigestion.
- Avoid foods with a high sugar content
- Avoid food colorings, preservatives and artificial additives.

Glossary of Terms

**Glycoprotein** Proteins with attached carbohydrates. The carbohydrates are short, branched chains, not polymers of repeating units of sugar residues.

**Glycolipid** Lipids with a chain of one or more amino sugar residue derivatives.

**Glycosaminoglycans** Carbohydrate chains made primarily of alternating of either NAG (N-acetylgalactosamine) plus glucuronic acid or its epimer iduronic acid. This category includes chondroitin, dermanatan, keratan, and heparen, almost always with sulfate groups attached.

**Hyaluronate** Often referred to as ‘the backbone of all proteoglycans. It is a chain of alternating residues of NAG and glucuronic acid.

**Proteoglycans** Giant molecules with many Glycosaminoglycans attached to a long strand of hyaluronate.

References


